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Breast Cancer among Hispanic Women

PRINCIPAL INVESTIGATOR: Gerson Peltz, M.D.

CONTRACTING ORGANIZATION: The University of Texas at Brownsville
Texas Southmost College
Brownsville, TX 78520-4956

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Introduction

The purpose of this Minority Institution Partnership Training Award is to train University of Texas at Brownsville (UTB) faculty to conduct breast cancer research by collaborating with faculty from the University of Texas-Houston School of Public Health (UTSPH). Three UTB faculty will undergo intensive training provided by six UTSPH faculty during year 1. Additional training will take place in subsequent years. To reinforce training, faculty from UTB and UTSPH will conduct a clinic-based case-control study of breast cancer to investigate its' association with hormones, diet and body size in years 2 through 4. Specific aims are: 1) to provide UTB faculty training through classes, presentations and seminars to gain knowledge of epidemiology, proposal development, cancer epidemiology, intervention mapping, field epidemiology, biostatistics, and nutrition epidemiology offered by UTSPH faculty in-person from Brownsville and via ITV from Houston, 2) to design and conduct a clinic-based case-control study to include completion of a questionnaire, anthropometry and a blood draw, 3) to disseminate findings to the Texas Department of Health, the Department of Defense, and local health providers and health clinics, and 4) to submit proposals to conduct larger population-based case-control studies of breast cancer in the Lower Rio Grande Valley.

Body

This project is occurring in two phases, the training phase (year 1) and the investigation phase (years 2 through 4). During the first year of the project, we partially completed training task 1 by Dr. Peltz (UTB) taking introductory epidemiology and behavioral sciences in Fall, 2003, and introductory biostatistics and nutritional epidemiology in Spring, 2004. Although Drs. Estrada (UTB) and Johnson (UTB) will not earn a Master's of Public Health degree, they audited proposal development in Spring, 2004. We completed training task 2 by Dr. Sanderson (UTSPH) co-chairing the Texas Cancer Registry Data Utilization Subcommittee to encourage timely reporting of breast cancer cases to the Texas Cancer Registry. We completed training task 3 by identifying Valley Baptist Medical Center and South Texas Hospital as the sites for the clinic-based case-control study, the South Texas Women's Health Project. We completed training task 4 by designing the South Texas Women's Health Project to include completion of a questionnaire, anthropometry and a blood draw. We completed training task 5 by combining questions from the standard breast cancer questionnaire, the National Health Interview Survey, and the questionnaire currently in use for the Four Corners Study which includes one-third Hispanic women. We completed training task 6 by designing the protocols for data collection, laboratory work, tracking system, data entry programs, and by writing the manual of operations. We completed training task 7 by obtaining institutional review board approval from the University of Texas at Brownsville on February 12, 2003, from Valley Baptist Medical Center on July 9, 2003, from the University of Texas Health Science Center at Houston on October 17, 2003, from Texas Department of Health the agency granting approval for South Texas Hospital on April 22, 2004, and from the Department of Defense on June 30, 2004. We completed training task 8 by piloting the procedures and questionnaire for the South Texas Women's Health Project at Valley Baptist Medical Center and mammography clinic from January 6, 2004 through present. We began interviewing at South Texas Hospital on August 2, 2004 to increase patient accrual. As of September 23, 2004 a total of 56 women receiving diagnostic mammograms (91.8% of eligible cases) and 110 women receiving screening mammograms (83.3% of eligible controls) had completed or were pending completion of a standardized in-person or telephone

interview. Dr. Sanderson (UTSPH) received funding from National Institutes of Health to conduct a pilot study of the clinic-based case-control study, thus the number of women included in the pilot study is much larger than we anticipated. Dr. Peltz (UTB) has applied for funding through the National Institutes of Health to add a urine collection component to the South Texas Women's Health Project to determine phytoestrogen excretion.

During the second year of the project we will move from the training phase into the investigation phase. We will partially complete training task 1 by Dr. Peltz (UTB) continuing to take coursework toward completion of the Master's of Public Health degree. Dr. Estrada (UTB) and Johnson (UTB) will audit an epidemiology and a behavioral sciences course, respectively. We will partially complete or complete investigation tasks 1 through 8. Investigation tasks 9 through 15 will be partially completed or completed in subsequent years.

Key Research Accomplishments

- Partially completed training task 1 by Dr. Peltz (UTB) taking epidemiology (introductory and nutrition), biostatistics, and behavioral sciences, and Drs. Estrada (UTB) and Johnson (UTB) auditing proposal development.
- Completed training task 2 by Dr. Sanderson (UTSPH) co-chairing the Texas Cancer Registry Data Utilization Subcommittee to encourage timely reporting of breast cancer cases to the Texas Cancer Registry.
- Completed training tasks 3 through 8 by identifying the sites and designing the South Texas Women's Health Project to include completion of a questionnaire, anthropometry and a blood draw; developing a questionnaire appropriate for use with the local Hispanic population; designing the protocols for data collection, laboratory work, tracking system, data entry programs, and by writing the manual of operations; obtaining institutional review board approval from several entities; conducting a pilot study, and revising the study design as needed. Dr. Sanderson (UTSPH) received additional funding to conduct a pilot study of the South Texas Women's Health Project. Dr. Peltz (UTB) applied for funding to add urinary excretion of phytoestrogen to the South Texas Women's Health Project.

Reportable Outcomes

1) Manuscripts

Coker AL, Sanderson M, Zheng W, Fadden MK. Diabetes mellitus and prostate cancer risk among older men: population-based case-control study. *Br J Cancer* 2004; 90:2171-2175.

Sanderson M, Coker AL, Logan P, Fadden MK, Zheng W. Lifestyle and prostate cancer among older African-American and Caucasian men in South Carolina. *Cancer Causes Control* 2004;15:647-655.

Sanderson M, Shu XO, Yu H, Dai Q, Malin AS, Gao Y-T, Zheng W. Insulin-like growth factor-I, soy protein intake and breast cancer risk. *Nutr Cancer* (In press).

2) Abstracts

Sanderson M, Coker AL, Logan P, Zheng W, Fadden MK. Lifestyle and prostate cancer among older African-American and Caucasian men in South Carolina. Am J Epidemiol 2004;159:S13.

Coker AL, Sanderson M, Zheng W, Fadden MK. Diabetes Mellitus and prostate cancer risk among older men: Population-based case-control study. Am J Epidemiol 2004;159:S8.

3) Grants

Name: Insulin Resistance and Breast Cancer
Funding Agency: National Institute of Minority Health and Health Disparities
Period of Funding: March 1, 2003 – February 28, 2005
Amount: \$84,000 (total direct)

Name: Urinary Excretion of Phytoestrogen in Breast Cancer among Hispanic Women
Funding Agency: National Institute of General Medical Sciences, MBRS-SCORE
Period of Funding: April 1, 2005 – March 31, 2006
Amount: \$49,828 (total direct)
Status: Pending

Conclusions

The overall goal of this Minority Institution Partnership Training Award is to further strengthen the collaborative relationship between the minority institution, UTB, and the collaborating institution, UTSPH. The UTSPH established a regional campus on the UTB campus in 2001, and the Co-Principal Investigator of the partnership from UTSPH is located in Brownsville. The vision of UTB and the UTSPH, Brownsville regional campus is to conduct community-based participatory research in areas deemed important by the community.

The training program will focus on breast cancer etiology, specifically the interrelationships between hormones, diet, body size and breast cancer among Hispanic women. The Lower Rio Grande Valley (LRGV) of Texas is an exceptional location to perform breast cancer research because 85 percent of the population is Hispanic. Hispanic women in the LRGV have a relatively low incidence of breast cancer compared with non-Hispanic white women. In comparison with Hispanic women in the US, Hispanic women residing in the LRGV have a higher mortality from breast cancer. In contrast, Hispanic women are at greater risk of insulin resistance. This research will allow us to investigate whether the reduced risk of breast cancer among Hispanic women in the LRGV may be related to their higher genetic susceptibility to insulin resistance. Women tend to develop insulin resistance if they are genetically susceptible, gain excess weight due to physical inactivity, and consume a high-fat, low-fiber diet during adolescence and adulthood. It is clear that this area of research has promise with regard to explaining the different breast cancer incidence and mortality rates by ethnicity. We hypothesize that the South Texas Women's Health Project conducted as part of the training program will be useful in identifying factors associated with decreased breast cancer risk among Hispanic women.

While faculty from UTSPH have expertise in breast cancer research, faculty from UTB have strong ties with the medical and lay community in Brownsville and Cameron County. To date, no breast cancer research has been conducted in Cameron County. By partnering together, these institutions hope to achieve the following goals: 1) develop a regional cancer registry, 2) build infrastructure to conduct population-based case-control studies of breast cancer, 3) initiate studies to investigate factors which may protect Hispanic women from breast cancer, and 4) establish an outstanding breast cancer research program.

References

Coker AL, Sanderson M, Zheng W, Fadden MK. Diabetes mellitus and prostate cancer risk among older men: population-based case-control study. *Br J Cancer* 2004; 90:2171-2175.

Sanderson M, Coker AL, Logan P, Fadden MK, Zheng W. Lifestyle and prostate cancer among older African-American and Caucasian men in South Carolina. *Cancer Causes Control* 2004;15:647-655.

Sanderson M, Shu XO, Yu H, Dai Q, Malin AS, Gao Y-T, Zheng W. Insulin-like growth factor-I, soy protein intake and breast cancer risk. *Nutr Cancer* (In press).

Statement of Work

Interrelationships of Hormones, Diet, Body Size and Breast Cancer among Hispanic Women

Phase 1: Training phase (Year 1)

- 1) Complete coursework toward Master's of Public Health degree
- 2) Liaise with local medical providers, health clinics and state health agencies to encourage reporting of breast cancer to the Texas Cancer Registry
- 3) Identify sites for data collection with local health providers and health clinics
- 4) After consultation with local health providers design a case-control study to include completion of a questionnaire, anthropometry and a blood draw
- 5) Develop a questionnaire appropriate for use with the local Hispanic population
- 6) Design protocols for data collection, laboratory work, tracking system, data entry programs, and write manual of operations
- 7) Initiate institutional review board approval through local and federal channels
- 8) Pilot test study methods and revise the study design as needed

Phase 2: Investigation Phase (Years 2 through 4)

- 1) Identify and recruit 500 breast cancer cases and 1000 controls identified by mammography centers
- 2) Complete questionnaires to obtain information on breast cancer risk factors, personal health history (e.g., type 2 diabetes), medication history (e.g., estrogen and insulin), and diet
- 3) Collect anthropometric measurements and pre-diagnostic blood
- 4) Abstract medical records for relevant health history and pathology data
- 5) Process and store blood samples
- 6) Complete enzyme-linked immunosorbent assays for insulin, insulin-like growth factor-I, insulin-like growth factor binding protein-3, and sex hormone-binding globulin, enzyme immunoassays for estradiol and estrone, and measure glucose on a biochemistry analyzer
- 7) Complete data entry of all questionnaires and assays
- 8) Perform interim statistical analyses at end of year 2 to assess data quality
- 9) Perform final statistical analyses to test study hypotheses
- 10) Consult with local health providers and health clinics regarding the cancer reporting mechanism and provide training as needed
- 11) Expand data collection to cancers other than breast cancer as a means of developing a regional Lower Rio Grande Valley cancer registry.
- 12) Disseminate findings to the Texas Department of Health, the Department of Defense, and local health providers and health clinics
- 13) Prepare manuscripts to report study results
- 14) Archive dataset for future analyses and future patient follow-up
- 15) Submit proposals to conduct larger population-based case-control studies of breast cancer in the Lower Rio Grande Valley

**Diabetes Mellitus and Prostate Cancer Risk among Older
African-American and Caucasian Men: Population-based Case-Control Study**

Ann L. Coker, PhD, Maureen Sanderson, PhD, Wei Zheng, PhD, Mary K. Fadden, MPH

Objective: to investigate the association between a past diabetes mellitus diagnosis and risk of prostate cancer among older (age 65-79) African-American and Caucasian men.

Design: Population-based case-control study.

Setting: Cases and controls were residents of South Carolina between 2000 and 2001.

Participants: 400 incident prostate cancer cases were ascertained through the South Carolina Central Cancer Registry, 389 controls were identified through the Health Care Financing Administration Medicare beneficiary file. Consenting participants completed telephone interviews (70% response rate) that addressed demographics, usual occupation, family history of prostate cancer, medical history, body mass index, diet, physical activity, drinking and smoking.

Main Outcome Measures: Incident histological confirmed prostate cancer

Results: After adjusting for age, education, body mass index, history of benign prostatic hyperplasia, family history of prostate cancer, and recent digital rectal prostate cancer screening, a history of diabetes mellitus was associated with a marked reduction in risk of prostate cancer for African-American men (adjusted Odds Ratio (aOR) = 0.29; 95% confidence interval (CI) = 0.16, 0.53) yet not for Caucasian men (aOR = 1.10; 95% CI = 0.61, 1.98). The protective effect was stronger for those with complications associated with diabetes (aOR=0.27; 95% CI = 0.14, 0.50) and for those diagnosed at an earlier stage (stage I-II: aOR = 0.26; 95% CI = 0.16, 0.49) again only for African-American men.

Conclusions: Ethnic differences in the impact of diabetes on subsequent prostate cancer risk suggest that genetic factors may play an important role in understanding this association.

**Lifestyle and Prostate Cancer among Older
African-American and Caucasian Men in South Carolina**

Maureen Sanderson, Ann L. Coker, Pamela Logan, Wei Zheng, Mary K. Fadden

Objective: We investigated the association between lifestyle and prostate cancer risk among Caucasian and African-American men, separately.

Methods: This population-based case-control study of prostate cancer among men aged 65-79 years was conducted between 2000 and 2002 in South Carolina. Telephone interviews were completed with 416 incident prostate cancer cases ascertained through the South Carolina Central Cancer Registry, and 429 controls identified through the Health Care Financing Administration Medicare beneficiary file (with respective response rates of 71% and 64%).

Results: Caucasian men working in production, transportation, and material moving had increased prostate cancer risk (odds ratio [OR]=2.04, 95% confidence interval [CI] 1.17-3.54), while African-American men in the military had reduced prostate cancer risk (OR=0.19, 95% CI 0.05-0.76). Having 5 or more prostate specific antigen (PSA) tests within the past 5 years was associated with prostate cancer among Caucasian men; however, African-American men with prostate cancer tended to have fewer PSA tests. Increasing lycopene consumption was associated with a reduced risk of prostate cancer among Caucasian men ($p=0.03$), but not among African-American men.

Conclusions: In this population-based case-control study conducted in South Carolina we did not find marked differences in lifestyle factors associated with prostate cancer by race.

Insulin-Like Growth Factor-I, Soy Protein Intake and Breast Cancer Risk

Maureen Sanderson, Xiao Ou Shu, Herbert Yu, Qi Dai, Alecia S. Malin, Yu-Tang Gao, Wei Zheng

Previous studies have found that estrogen enhances the effect of insulin-like growth factor-I (IGF-I) levels on breast cancer cell growth. Participants in the Shanghai Breast Cancer Study (SBCS) consume large amounts of soy that is high in isoflavones, which act as weak estrogens and as anti-estrogens. We assessed whether soy protein intake modified the effect of IGF-I levels on breast cancer risk. The SBCS is a population-based case-control study of breast cancer among women aged 25 to 64 conducted between 1996 and 1998 in urban Shanghai. In-person interviews were completed with 1459 incident breast cancer cases ascertained through a population-based cancer registry, and 1556 controls randomly selected from the general population (with respective response rates of 91% and 90%). This analysis is restricted to the 397 cases and 397 matched controls for whom information on IGF-I levels was available. For premenopausal breast cancer, we found nearly significant interactions between soy protein intake and IGF-I levels ($p=0.080$) and insulin-like growth factor binding protein-3 (IGFBP-3) levels ($p=0.057$). The direction of the interaction appeared to be negative for IGF-I levels, but was positive for IGFBP-3 levels. No interaction was evident between soy protein intake and IGF-I or IGFBP-3 levels among postmenopausal women. Our results suggest that soy protein intake may negatively modulate the effect of IGF-I and may positively modulate the effect of IGFBP-3 levels on premenopausal breast cancer risk. Further studies are needed to confirm our finding and to understand the biological mechanisms of these potential interactions.

Insulin Resistance and Breast Cancer

Maureen Sanderson, PI

The primary purpose of this proposed pilot study is to investigate the association between insulin resistance and breast cancer risk. We hypothesize that 1) insulin resistance, defined as high levels of insulin and glucose or type 2 diabetes, will be positively associated with breast cancer, and 2) the insulin resistance-breast cancer association will be more pronounced among women with abdominal obesity and high levels of estradiol (E2). The specific aims of the proposed case-control study are: 1) to obtain information on type 2 diabetes, waist and hip circumference, body mass index, body fat content, birth weight, age at which adult height was achieved, diet, physical activity, and weight gain, and to collect pre-diagnostic blood, 2) to assay blood for E2, sex hormone-binding globulin, insulin, glucose, and triglycerides, and 3) to perform statistical analyses to assess the association between insulin resistance and breast cancer risk, while accounting for confounding and interaction. This proposed study will be conducted in three mammographic centers. We plan to recruit 390 incident breast cancer cases and 390 control women. Breast cancer cases will be those women identified as having breast cancer through diagnostic mammography prior to undergoing treatment. Control women will be those women who are cancer free through screening mammography. In addition, control women will be at low risk of breast cancer defined as having no previous lesions that place her at higher than minimal risk, and no first-degree relative with a history of breast cancer or other hormone-related cancer. Insulin resistance may be associated with breast cancer, and may help explain the elevated risk of breast cancer among certain ethnic groups. Despite being at greater risk of insulin resistance, Hispanic women have a relatively low incidence of breast cancer. This proposed study may be useful in identifying factors associated with decreased breast cancer risk among Hispanic women.

Urinary Excretion of Phytoestrogen and Breast Cancer among Hispanic Women

Gerson Peltz, PI

Phytoestrogen intake, measured as dietary consumption of phytoestrogens or as urinary excretion of phytoestrogens, has been found to be protective against breast cancer, especially in populations that consume large amounts of soy. Despite possessing many risk factors for breast cancer, Hispanic women have a relatively low incidence of the disease. A possible explanation for the lower risk of breast cancer among Hispanic women is their high consumption of grains rich in phytoestrogens. We hypothesize that high phytoestrogen intake, as measured by urinary excretion of phytoestrogen, will be protective against breast cancer in a population of Hispanic women. We propose to add urine collection and assessment of urinary excretion of phytoestrogen, another measure of phytoestrogen intake to the ongoing South Texas Women's Health Project, to more accurately reflect consumption of phytoestrogen-rich foods by women in our population. Specific aims of the proposed pilot project are: 1) to determine phytoestrogen intake by measuring urinary excretion of phytoestrogens on a sub-sample of 400 cases and 400 controls participating in our ongoing case-control study of breast cancer, 2) to investigate association between dietary consumption of phytoestrogen, urinary excretion of phytoestrogen, and blood levels of hormones and growth factors among controls, and 3) to evaluate whether phytoestrogen intake reduces breast cancer risk. We will add urine collection from subjects to the ongoing South Texas Women's Health Project. We will perform assays on urinary excretion of phytoestrogen on a sub-sample of 400 cases and 400 controls. We will conduct statistical analyses to evaluate phytoestrogen intake and its relation with hormones, growth factors and breast cancer. The proposed pilot project to be conducted within an ongoing case-control study will be one of very few breast cancer studies that have focused on Hispanic women. The

Appendix F

PRINCIPAL INVESTIGATOR: Peltz, Gerson

identification of protective factors against breast cancer among Hispanic women may contribute to our understanding of the biological mechanisms of the disease.